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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 13-MAY-1999

SUBJECT: ID#99MT0012. SECTION 18 EXEMPTION FOR THE USE OF **PYRIDATE** ON **MINT** IN **MONTANA**.

DP Barcode:	D254479	EPA Reg#:	100-877
Submission #:	S558560	PRAT Case#:	291638
Chemical#:	128834	Class:	Fungicide
Trade Name:	Tough 5EC	40 CFR:	180.462

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INTRODUCTION

The Montana Department of Agriculture is proposing a Section 18 exemption for the use of pyridate (formulated as Tough 5EC) on mint for control of kochia and redroot pigweed. Tough 5EC will be applied to a maximum of 3,600 acres in Montana from May 1 through December 31, 1999. This document addresses the human health risks associated with the use of pyridate on mint. This is the first §18 request for this use.

SUMMARY

Tough 5EC is a Novartis product containing 55.8% of the a.i. pyridate. Tolerances have been established for the residues of pyridate (O- (6-chloro-3-phenyl-4-pyridazinyl) -S-octyl-carbonothioate), its metabolite 6-chloro-3-phenyl-pyridazine-4-ol (aka CL9673), and conjugates of that metabolite, all expressed as pyridate in or on the following raw agricultural commodities (40 CFR §180.462(a)): cabbage at 0.03 ppm; chickpeas at 0.1 ppm; corn, fodder at 0.03 ppm; corn, forage at 0.03 ppm; corn, grain at 0.03 ppm; corn, silage at 0.03 ppm; and peanut, nutmeat at 0.03 ppm..

On October 21, 1997, the HIARC evaluated the toxicology database, selected doses and endpoints for acute and chronic dietary, as well as occupational and residential exposure risk assessments, assessed the carcinogenic potential, and addressed the sensitivity of infants and children from exposure to pyridate as required by the Food Quality Protection Act (FQPA) of 1996. For dietary exposure, the HIARC selected an acute RfD of 0.2 mg/kg/day (NOAEL = 20.0 mg/kg/day, UF =100). The acute RfD is based on neurotoxic effects observed in a 90-day feeding study in dogs at 60 mg/kg/day (LOAEL). The HIARC selected a chronic RfD of 0.11 mg/kg/day (NOAEL = 10.8 mg/kg/day, UF =100). The chronic RfD is based on decreased body weight gain in males observed in a 2-year feeding study in rats at 67.5 mg/kg/day (LOAEL).

The HIARC selected short- and intermediate-term dermal endpoints from a 90-day feeding study in dogs. The NOAEL of 20.0 mg/kg/day was based on neurotoxic effects (ataxia and emesis) observed at 60 mg/kg/day (LOAEL). A long-term dermal endpoint was chosen from a 2-year rat feeding study. The NOAEL of 10.8 mg/kg/day was based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL). Since oral doses were selected for dermal risk assessments, a dermal penetration of 20% was established. The HIARC selected oral NOAELs for inhalation risk assessments. The HIARC recommended (1) converting inhalation exposure in mg/L to mg/kg/day (route-to-route extrapolation using 100% inhalation absorption), (2) combining the converted exposure with dermal exposure (using 20% dermal absorption) and (3) comparing the combined total to the appropriate oral NOAEL chosen for the short- and intermediate-term exposure scenario (NOAEL = 20 mg/kg/day) or chronic term exposure scenario (NOAEL = 10.8 mg/kg/day).

On April 5,1999, the FQPA Safety Factor Committee (SFC) met and determined that the 10x factor to account for enhanced sensitivity of infants and children should be removed (i.e. reduced to 1x). For acute and chronic dietary risk assessments, an UF of 100 is adequate for the protection of the general U.S. population including infants and children from exposure to pyridate. **Please note: the decisions made at the 4/5/99 meeting for pyridate are applicable only to this Section 18 request** (Memo, B. Tarplee 4/8/99). The acute and chronic Population Adjusted Doses (aPAD and cPAD) are modifications of the acute and chronic RfDs to accommodate the FQPA Safety Factor. The PAD is equal to the acute or chronic RfD divided by the FQPA Safety Factor. **Since the HED FQPA SFC determined to remove the 10x safety factor (i.e. reduce to 1x), the RfD is identical to the PAD.**

Pyridate has not been to the Cancer Peer Review Committee (CPRC). However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97).

The Environmental Fate and Effects Division (EFED) has provided HED with estimated drinking water environmental concentrations (DWECs) of pyridate in ground and surface water (Memo, F. Jenkins 4/16/99; Barcode D254476). EFED estimates acute and chronic DWECs for ground water (using SCI-GROW) at 4.44 ppb. They also estimated acute and chronic (56-day) DWECs for surface water (using GENEEC) at 97 ppb and 75 ppb, respectively. According to HED drinking water guidance (HED SOP 98.4) the 90/56-day GENEEC value may be divided by 3 to obtain a value for chronic risk assessment calculations. Therefore, the surface water value for use in the chronic risk assessment would be **25 ppb**.

The Agency has identified toxicological endpoints of concern for occupational and residential exposure. Handler exposures addressing mixer/loaders and applicators have been assessed using surrogate data available in the Pesticide Handlers Exposure Database (PHED Ver 1.1). The HIARC recommended 100 as the level of concern for estimating Margins of Exposure (MOEs) for occupational and residential exposures. An MOE of 100 is adequate to ensure protection for handler exposure to pyridate via the dermal and inhalation routes. Since no potentially significant post-application exposure is expected based on the use patterns, this exposure assessment was not warranted. Pyridate is applied twice per year and only short-term exposure is expected from the proposed uses. Although pyridate has not been classified by the HIARC Committee or the CPRC, there was no evidence of carcinogenic potential in the 2-year rat feeding study and the mouse carcinogenicity study. Therefore, a cancer risk assessment is not required. **All occupational exposure scenarios yield risk estimates below HED's level of concern for pyridate.** There are no residential uses, nor are there any occupational uses resulting in non-dietary exposure to infants and children, at this time.

Acute aggregate risk estimates do not exceed HED's level of concern. For the U.S. population and all subgroups, including infants and children, <1% of the aPAD is occupied by dietary (food) exposure. The estimated average concentrations of pyridate in surface and ground water are less than HED's levels of comparison for pyridate in drinking water as a contribution to acute aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of pyridate in drinking water do not contribute significantly to the acute aggregate human health risk at the present time considering the present uses and uses proposed in this action.

Chronic aggregate risk estimates do not exceed HED's level of concern. For the U.S. population and all subgroups, including infants and children, <1% of the cPAD is occupied by dietary (food) exposure. The estimated average concentrations of pyridate in surface and ground water are less than HED's levels of comparison for pyridate in drinking water as a contribution to chronic aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of pyridate in drinking water do not contribute significantly to the chronic aggregate human health risk at the present time considering the present uses and uses proposed in this action.

The toxicological, chemistry and occupational /residential exposure databases are adequate to support the following time-limited tolerance and Section 18 registration for the use of pyridate in/on mint in terms of human health risk:

Peppermint, tops (leaves and stems)	-	0.3 ppm
Spearmint, tops (leaves and stems)	-	0.3 ppm

TOXICOLOGICAL ENDPOINTS

On October 21, 1997, the HIARC evaluated the toxicology database, selected doses and endpoints for acute and chronic dietary, as well as occupational and residential exposure risk assessments, assessed the carcinogenic potential, and addressed the sensitivity of infants and children from exposure to pyridate as required by the FQPA. The data in the following toxicity profile for this risk assessment have been obtained from HED reviews, including the HIARC document (Memo, J. Rowland 11/3/97).

1. Dietary Exposure

Acute Dietary. **Acute RfD = 0.20 mg/kg/day**. For acute dietary risk assessment, the HIARC recommended use of the systemic NOAEL of 20 mg/kg/day based on neurotoxic effects (ataxia and emesis) seen at 60 mg/kg/day (LOAEL) in the 90-day feeding study in dogs (MRID# 40101604). An uncertainty factor of 100 (10x for interspecies differences and 10x for intraspecies variations) was used to determine the acute RfD of 0.20 mg/kg/day.

Chronic Dietary. **Chronic RfD = 0.11 mg/kg/day**. For chronic dietary risk assessment, a NOAEL of 10.8 mg/kg/day was used based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL) in a 2-year feeding study in rats (MRID# 00137289, -90, 00138638). An uncertainty factor of 100 (10x for interspecies differences and 10x for intraspecies variations) was incorporated. The chronic study was supported by the parental systemic toxicity NOAEL and LOAEL established in the three-generation reproduction study in rats (MRID# 0072347). In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations).

2. Non-Dietary Exposure

Short and Intermediate-Term Exposure. For short and intermediate-term MOE calculations, the HIARC recommended use of the systemic NOAEL of 20 mg/kg/day from the 90-day feeding study in dogs (MRID# 40101604). At the LOAEL of 60 mg/kg/day, there were clinical signs of neurotoxicity.

Chronic Exposure. The HIARC recommended use of the NOAEL of 10.8 mg/kg/day from a 2-year feeding study in rats (MRID# 00137289, -90, 00138638) based on decreased body weight gain at the LOAEL of 67.5 mg/kg/day for chronic MOE calculations.

Dermal Penetration. A dermal absorption study was not available for evaluation. Therefore, HIARC estimated a dermal absorption rate of 20% percent based on the interpretation of data from oral and dermal studies in rats. In the oral developmental toxicity study in rat, the maternal NOAEL was 165 mg/kg/day based on mortality, significantly decreased mean body weight and food consumption and clinical signs observed at the NOAEL of 400 mg/kg/day. In the dermal toxicity study in rats, no

dermal or systemic toxicity was observed at the Limit-Dose of 1000 mg/kg/day (NOAEL).

In extrapolating from oral to dermal route, the HIARC made the following assumptions: 1) that the toxicity seen via the oral route is due to direct transport of pyridate from the absorption site to the target organs and 2) that metabolism following oral and dermal routes are similar. Under these assumptions, no more than 16% (oral NOAEL of 165 mg/kg/day ÷ dermal NOAEL 1000 mg/kg/day x 100) of pyridate applied to the rat skin is absorbed without effects. Due to the uncertainties in extrapolating from the oral to dermal route from the available data, HIARC decided to use a conservative dermal absorption value of 20% in the absence of definitive dermal absorption data.

Inhalation Toxicity. The HIARC selected oral NOAELs for inhalation risk assessments. The HIARC recommended (1) converting inhalation exposure from mg/L to mg/kg/day (route-to-route extrapolation using 100% inhalation absorption), (2) combining the converted exposure with dermal exposure (using 20% dermal absorption) and (3) comparing the combined total to the appropriate oral NOAEL chosen for the short- and intermediate-term exposure scenario (NOAEL = 20 mg/kg/day) or chronic exposure scenario (NOAEL = 10.8 mg/kg/day).

3. Cancer

Pyridate has not been classified by the HIARC or the CPRC. However, there is no evidence of a tumorigenic response in the 2-year rat feeding study and the mouse carcinogenicity study with pyridate.

4. Special Sensitivity to Infants and Children

In assessing the potential for additional sensitivity of infants and children to residues of **pyridate**, HED considered data from developmental toxicity studies in the rat and rabbit and a 2-generation reproductive toxicity study in the rat. Developmental toxicity studies are designed to evaluate adverse effects on the developing fetus resulting from maternal pesticide exposure during gestation. Reproductive toxicity studies provide information relating to pre- and post-natal effects from exposure to the pesticide, information on the reproductive capability of mating animals, and data on systemic toxicity.

Federal Food, Drug and Cosmetic Act (FFDCA) section 408 provides that EPA shall apply an additional 10-fold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a margin of exposure analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. In either case, EPA generally defines the level of appreciable risk as exposure that is greater than 1/100 of the no observed effect level in the animal study appropriate to the particular risk assessment. This 100-fold uncertainty (safety) factor/margin of exposure (safety) is

designed to account for inter-species extrapolation and intra-species variability. HED believes that reliable data support using the 100-fold margin/factor, rather than the 1000-fold margin/factor, when EPA has a complete data base under existing guidelines, and when the severity of the effect in infants or children, the potency or unusual toxic properties of a compound, or the quality of the exposure data do not raise concerns regarding the adequacy of the standard margin/factor.

a. Developmental Toxicity Studies.

1. Rats. In a prenatal developmental toxicity study in Wistar/HAN rats (MRID# 00158483), pyridate in carboxymethylcellulose was administered at doses of 0, 55, 165, or 400 mg/kg/day by gavage on gestation days 6-15. For maternal toxicity, the NOAEL was 165 mg/kg/day and the LOAEL was 400 mg/kg/day based on mortality, significant decreases in mean body weight and food consumption as well as clinical signs (ventral body position, dyspnea, sedation, and loss of reaction to external stimuli). The developmental NOAEL was 165 mg/kg/day and the developmental LOAEL was 400 mg/kg/day, based on increased incidences of missing and/or unossified sternebrae and a dose-related decrease in mean fetal body weight.

2. Rabbits. A prenatal developmental toxicity study was conducted in pregnant New Zealand white rabbits (MRID# 40463201), in which pyridate (neat) was administered by gavage at doses of 0, 150, 300 or 600 mg/kg/day on gestation days 7-19. For maternal toxicity, the NOAEL was 300 mg/kg/day and the LOAEL was 600 mg/kg/day, based on decreased body weight and body weight gain, decreased food consumption, increased incidence of dried feces, and increased abortions. For developmental toxicity the NOAEL was $\geq$ 600 mg/kg/day (HDT); a LOAEL was not established.

b. Reproductive Toxicity Studies.

1. Rats. In a three-generation reproduction study (MRID# 0072347), Sprague-Dawley rats received diets containing pyridate at doses of 0, 80, 400 or 2500 ppm (0, 2.2, 10.8 or 67.5 mg/kg/day, respectively). Each generation of rats was mated to produce two litters. The parental systemic NOAEL was 400 ppm (10.8 mg/kg/day) and the LOAEL was 2500 ppm (67.5 mg/kg/day) based on depression of maternal body weight gain. The NOAEL for offspring was 400 ppm (10.8 mg/kg/day) and the LOAEL was 2500 ppm (67.5 mg/kg/day) based on decreased pup weight gains (at postnatal day 14 and 21 in the first litters for both generations

c. Pre- and Post-Natal Sensitivity.

The toxicological data base for evaluating pre- and post-natal toxicity for pyridate is complete with respect to current data requirements. There are no pre- or post-natal toxicity concerns for infants and children, based on the results of the rat

and rabbit developmental toxicity studies and the 2-generation rat reproductive toxicity study. The FQPA SFC (4/5/99) recommended that the **10x FQPA Safety Factor should be removed (i.e. reduced to 1x)**.

Table 1

EXPOSURE DURATION	EXPOSURE ROUTE	DOSE and ENDPOINT
Acute (1-day)	Oral (Dietary)	RfD: 0.20 mg/kg/day NOAEL:20 mg/kg/day based on clinical signs indicative of neurotoxicity (ataxia and emesis) in dogs at a LOAEL of 60 mg/kg/day. UF = 100 (includes FQPA considerations).
Short-Term (1-7 days) Occupational/Residential	Dermal and Inhalation	Short and Intermediate Dermal and Inhalation NOAEL:20 mg/kg/day based on clinical signs indicative of neurotoxicity (ataxia and emesis) in dogs at a LOAEL of 60 mg/kg/day. MOE = 100
Intermediate-Term (1 week - several months) Occupational/Residential	Dermal and Inhalation	See Short-Term Occupational/Residential
Chronic-Term (several months-lifetime) Occupational/Residential	Dermal and Inhalation	NOAEL: 10.8 mg/kg/day based on decreased body weight gain in male rats at the LOAEL of 67.5 mg/kg/day. MOE = 100 Supported by parental systemic toxicity NOAEL and LOAEL established in the Three-Generation reproduction study in rats. In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations).
Cancer	Oral	Unclassified. Negative in mice and rats.
Chronic (non-cancer)	Oral	RfD: 0.11 mg/kg/day NOAEL:10.8 mg/kg/day based on decreased weight gain in male rats at the LOAEL of 67.5 mg/kg/day. MOE = 100 Supported by parental systemic toxicity NOAEL and LOAEL established in the Three-Generation reproduction study in rats. In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations).

DIETARY AND RESIDENTIAL EXPOSURES AND RISKS

In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency considers include drinking water (whether from ground or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor and/or outdoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

1. From Food and Feed Uses:

Dietary Exposure Evaluation Model (DEEM™) analysis for pyridate was performed in order to provide an estimate of the dietary exposure and associated risk for pyridate resulting from existing tolerances and proposed tolerance levels for mint (Memo, J. Rowell 5/10/99; Barcode D255654). The DEEM™ analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-92 Nationwide Continuing Surveys for Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The DEEM™ analysis is attached (Attachment 1).

The acute and chronic Population Adjusted Doses (aPAD and cPAD) are modifications of the acute and chronic RfDs to accommodate the FQPA Safety Factor. The PAD is equal to the acute or chronic RfD divided by the FQPA Safety Factor. **Since the HED FQPA SFC determined to remove the 10x safety factor (i.e. reduce to 1x), the RfD is identical to the PAD.**

a. Acute Risk

An acute dietary risk assessment is required for pyridate. The aPAD used for the acute dietary analysis for pyridate was 0.20 mg/kg bwt/day. A Tier 1 acute analysis was performed using published and proposed tolerance levels and 100% crop treated (CT) information for all commodities. For acute dietary risk, HED's level of concern is for exposures >100% aPAD. Dietary exposures and associated acute risk at the 95th percentile are shown in Table 2. The other subgroups included in Table 2 represent the highest dietary exposures for their respective subgroups (i.e., children, females, and the other general population subgroups higher than U.S. population).

Table 2- Summary of Results of Acute DEEM Analysis for Pyridate at the 95th Percentile.

Subgroup	Exposure (mg/kg/day)	% aPAD
U.S. Population (48 states)	0.000139	<1
Non-Hispanic Blacks	0.000159	<1
Non-nursing Infants (<1 yr)	0.000277	<1
Females (13+/nursing)	0.000124	<1

The results of the acute analyses indicate that the acute dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

b. Chronic Risk

A chronic dietary risk assessment is required for pyridate. The cPAD used for the chronic dietary analysis for pyridate is 0.11 mg/kg bwt/day. The chronic dietary exposure analysis used mean consumption (3-day average) data. A Tier 1 analysis was performed using published and proposed tolerance level residues and 100% CT information for all commodities. For chronic dietary risk, HED's level of concern is for exposures >100% cPAD. Dietary exposures for the General Population and other subgroups are presented in Table 3. The other subgroups included in Table 3 represent the highest dietary exposures for their respective subgroups (i.e., children, females, and the other general population subgroups higher than U.S. population).

Table 3. Summary of Results from Chronic DEEM Analysis of Pyridate.

Subgroup	Exposure (mg/kg/day)	% cPAD
U.S. Population (48 states)	0.000044	<1
Non-Hispanic Blacks	0.000050	<1
Non-nursing Infants	0.000121	<1
Females 13-19 (not preg or nursing)	0.000043	<1
Males 13-19 yrs	0.000054	<1

The results of the chronic analysis indicate that the chronic dietary risk associated with the existing and proposed uses of pyridate is below the Agency's current level of concern.

c. Cancer Risk

Pyridate has not been to the CPRC. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97). Therefore, no cancer dietary exposure analysis was performed.

2. From Drinking Water:

A Drinking Water Level of Comparison (DWLOC) is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxic endpoint, with drinking water consumption, and body weights. Different populations will have different DWLOCs.

HED uses DWLOCs internally in the risk assessment process as a surrogate measure of potential exposure associated with pesticide exposure through drinking water. In the absence of monitoring data for pesticides, it is used as a point of comparison against conservative model estimates of a pesticide's concentration in water.

DWLOC values are not regulatory standards for drinking water. They do have an indirect regulatory impact through aggregate exposure and risk assessments.

HED does not have monitoring data available to perform a quantitative drinking water risk assessment for pyridate at this time. EFED provided ground and surface water exposure estimates for the use of pyridate on mint (Memo, F. Jenkins 4/16/99; Barcode D254476). A previous memo for the estimated environmental concentrations of the use of pyridate on garbanzo beans in Idaho was completed (Memo: Pyridate Environmental Fate Characteristics and Estimated Ground Water and Surface Water Concentrations Resulting from Proposed Use on Garbanzo Beans: Chemical No. 128834; DP Barcode D223398; Case 287340; ID 6E04667). The application rate of 0.9 lbs./acre and number of application (2 applications) for the garbanzo bean use are equal to the maximum application rate and maximum number of applications for the proposed use on mint. Therefore, EFED assumes that the estimated environmental concentrations are expected to be equal for both the garbanzo bean use and proposed mint use. The following information has been extrapolated from the previous garbanzo bean use memo (Memo, F. Jenkins 4/16/99; Barcode D254476).

a. Ground Water (tiered assessment)

A ground water estimate was made using the SCI-GROW screening model. EFED calculated the following for pyridate in ground water: **4.4 ppb**. This concentration may be used for both the acute and chronic values.

b. Surface Water (tiered assessment)

Acute and chronic (56-day) DWECs for surface water The GENEEC estimated to be 97 ppb and 75 ppb, respectively. According to HED drinking water guidance (HED SOP 98.4) the 90/56-day GENEEC value may be divided by 3 to obtain a value for chronic risk assessment calculations. Therefore, the surface water value for use in the chronic risk assessment would be **25 ppb**.

c. Environmental Fate Assessment

Pyridate generally hydrolyzes to a major degradate, CL-9673, and several minor degradates. In summary, the data indicate that in terrestrial and aquatic environments, pyridate rapidly hydrolyzes to CL-9673 with half lives usually $\leq$3 days. Although pyridate is also rapidly hydrolyzed under anaerobic soil conditions to CL-9673, CL-9673 is persistent and undergoes very little degradation with half lives from 330-630 days in anaerobic soil conditions. Aerobic half lives of CL-9673 are about 10-30 weeks in soils (incorrectly given as 10-30 days in the EPA one-liner database). CL-9673 is rapidly degraded under the influence of light as indicated by the 14 day half life in the water and 16 day half life in soil. In general, pyridate and its primary degradate, CL-9673, will not persist in aerobic conditions, while CL-9673 will persist in anaerobic conditions.

d. Drinking Water Risk (Chronic)

HED has calculated DWLOCs and the results are listed in Tables 4 and 5.

Table 4. Summary of DWLOC Calculations - Acute Scenario.

Population Subgroup[1]	Acute Scenario					
	Food Exposure mg/kg/day	% aPAD	Maximum Water Exposure mg/kg/day[2]	SCI-GROW (ppb)[3]	GENEEC (ppb)	DWLOC (ppb)
U.S. Population (48 states)	0.000139	<1	0.19986	4.4	97	7000
Non-Hispanic Blacks	0.000159	<1	0.19984	4.4	97	7000
Non-nursing Infants (<1 yr)	0.000278	<1	0.19991	4.4	97	2000
Females (13+/nursing)	0.000124	<1	0.19988	4.4	97	6000

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed), the female subgroup with the highest food exposure (60 kg. body weight assumed), the other general population subgroup (70 kg body weight assumed) which has higher dietary exposure than the U.S. population, and the infant/child subgroup with the highest food exposure (10 kg. body weight assumed).

[2]Maximum Water Exposure (mg/kg/day) = aPAD (mg/kg/day) - Dietary Exposure from DEEM (mg/kg/day)

[3]The crop producing the highest level was used.

Table 5. Summary of DWLOC Calculations - Chronic (Non-Cancer) Scenario.

Population Subgroup[1]	Chronic (Non-Cancer) Scenario					
	Food Exposure mg/kg/day	% cPAD	Maximum Water Exposure mg/kg/day[2]	SCI-GROW (ppb)[3]	GENEEC (ppb)	DWLOC (ppb)
U.S. Population (48 states)	0.000044	<1	0.10996	4.4	25	3800
Non-Hispanic Blacks	0.000050	<1	0.10995	4.4	25	3800
Non-nursing Infants	0.000121	<1	0.10988	4.4	25	1100
Females 13-19 (not preg/not nursing)	0.000043	<1	0.10996	4.4	25	3300

[1]Population subgroups chosen were U.S. population (70 kg. body weight assumed), the female subgroup with the highest food exposure (60 kg. body weight assumed), the other general population subgroup (70 kg body weight assumed) which has higher dietary exposure than the U.S. population, and the infant/child subgroup with the highest food exposure (10 kg. body weight assumed).
[2]Maximum Water Exposure (mg/kg/day) = cPAD (mg/kg/day) - Dietary Exposure from DEEM (mg/kg/day)
[3]The crop producing the highest level was used.

To calculate the DWLOC for acute exposure relative to an acute toxicity endpoint, the acute dietary food exposure (from DEEM™) was subtracted from the aPAD to obtain the acceptable acute exposure to pyridate in drinking water. To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DEEM™) was subtracted from the cPAD to obtain the acceptable chronic (non-cancer) exposure to pyridate in drinking water. DWLOCs were then calculated using the following default body weights and drinking water consumption figures, which are listed in Table 6.

Table 6. Default Body Weight and Drinking Water Consumption Figures

DEEM Population	Body Weights (kg)	Drinking Water Consumption (liters/day)
U.S. Population/48 States	70	2
Females 13+	60	2
Infants/children	10	1

Calculation (for acute and chronic exposures):

$$DWLOC\ (\mu g/L) = \frac{water\ exposure\ (mg/kg/day)\ x\ (body\ weight)}{consumption\ (L)\ x\ 10^{-3}\ mg/\mu g}$$

The estimated average concentrations of pyridate in surface water are 97 ppb (acute exposure) and 25 ppb (chronic exposure). The estimated average concentration of pyridate in groundwater is 4.4 ppb (acute and chronic exposures). The estimated acute and chronic concentrations of pyridate in surface water and groundwater are less than HED's DWLOCs for pyridate as a contribution to acute and chronic aggregate exposure. Therefore, taking into account the present uses and uses proposed in this action, HED concludes with reasonable certainty that residues of pyridate in drinking water (when considered along with other sources of exposure for which HED has reliable data) would not result in unacceptable levels of acute or chronic aggregate human health risk at this time.

HED bases this determination on a comparison of estimated concentrations of pyridate in surface waters and ground waters to back-calculated DWLOCs for pyridate. These DWLOCs were determined after HED has considered all other non-occupational human exposures for which it has reliable data, including all current uses, and uses considered in this action. The estimates of pyridate in surface waters are derived from water quality models that use conservative assumptions (health-protective) regarding the pesticide transport from the point of application to surface and ground water. Because HED considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, DWLOC may vary as those uses change. If new uses are added in the future, HED will reassess the potential impacts of pyridate on drinking water as a part of the aggregate risk assessment process.

3. From Residential Exposure:

There are no currently registered or proposed residential uses for pyridate.

DETERMINATION OF SAFETY FOR U.S. POPULATION

1. Acute Aggregate Risk

Since there are no residential uses for pyridate, the acute aggregate exposure includes only food and water.

Acute risk estimates resulting from aggregate exposure to pyridate in food and water are below HED's level of concern. For the U.S. population and all subgroups, including infants and children, <1% of the aPAD is occupied by dietary (food) exposure. The estimated average concentrations of pyridate in surface and ground water are less than HED's levels of comparison for pyridate in drinking water as a contribution to acute aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of pyridate in drinking water do not contribute significantly to the acute aggregate human

health risk at the present time considering the present uses and uses proposed in this action.

HED bases this determination on a comparison of estimated concentrations of pyridate in surface waters and ground waters to levels of comparision for pyridate in drinking water. The estimates of pyridate in surface and ground waters are derived from water quality models that use conservative assumptions regarding the pesticide transport from the point of application to surface and ground water. Because HED considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of comparision in drinking water may vary as those uses change. If new uses are added in the future, HED will reassess the potential impacts of pyridate on drinking water as a part of the acute aggregate risk assessment process.

2. Chronic Aggregate Risk

Since there are no residential uses for pyridate, the chronic aggregate exposure includes only food and water.

Chronic risk estimates resulting from aggregate exposure to pyridate in food and water are below HED's level of concern. For the U.S. population and all subgroups, including infants and children, <1% of the cPAD is occupied by dietary (food) exposure. The estimated average concentrations of pyridate in surface and ground water are less than HED's levels of comparision for pyridate in drinking water as a contribution to chronic aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of pyridate in drinking water do not contribute significantly to the chronic aggregate human health risk at the present time considering the present uses and uses proposed in this action.

HED bases this determination on a comparison of estimated concentrations of pyridate in surface waters and ground waters to levels of comparision for pyridate in drinking water. The estimates of pyridate in surface and ground waters are derived from water quality models that use conservative assumptions regarding the pesticide transport from the point of application to surface and ground water. Because HED considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of comparision in drinking water may vary as those uses change. If new uses are added in the future, HED will reassess the potential impacts of pyridate on drinking water as a part of the chronic aggregate risk assessment process.

3. Short- and Intermediate-Term Aggregate Risk

Since there are no residential uses or exposure scenarios, short- and intermediate-term aggregate risk assessments were not conducted.

4. Long-Term Aggregate Risk

Since there are no residential uses or exposure scenarios, short- and intermediate-term aggregate risk assessments was not conducted.

DETERMINATION OF CANCER RISK

Pyridate has not been classified by the HIARC or the CPRC. However, there is no evidence of a tumorigenic response in the 2-year rat feeding study and the mouse carcinogenicity study with pyridate (Memo, A. Kocialski, et. al. 7/11/97).

ENDOCRINE DISRUPTOR EFFECTS

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disruptor effects.

OCCUPATIONAL EXPOSURE AND RISK ASSESSMENT/CHARACTERIZATION

1. Summary of Use Patterns and Formulations

The state of Montana proposes the use of the active ingredient pyridate on mint crops for this Section 18 request. Tough 5EC (containing 55.8% of pyridate), is an emulsifiable concentrate used for post-emergent weed control. Pyridate will be applied by ground equipment to control kochia and redroot pigweed on mint (aerial application is strictly prohibited by label restrictions). It will be applied to a maximum of 3,600 acres in Montana from May 1 through December 31, 1999. Two applications each at a maximum rate of 0.94 lbs ai/A will be made. The applications will by made at 14-day intervals. No applications will be made within 49 days of harvest.

Table 7. Use Pattern Summary of Pyridate (in Tough 5EC) on Mint

Factors	Quantities
Formulation	emulsifiable concentrate
Crop to be treated	mint
Pests	redroot pigweed, kochia
Application methods	groundboom sprayer
Maximum application rate (AR)	0.94 lb a.i. per acre.
Maximum number of applications	2 applications made a minimum of 14 day intervals
Total Amount of Pesticide to be Used	6,750 lbs ai
Use Period	1 May - 31 December 99
Total Acres to be Treated	3,600
Manufacturer	Novartis

2. Occupational and Residential Exposures and Assumptions

a. Handler Exposure Assumptions

HED has identified toxicological endpoints of concern for occupational and residential exposure. Handler exposure addressing mixer/loaders and applicators have been assessed using surrogate data available in the Pesticide Handlers Exposure Database (PHED Ver 1.1, 1997) Surrogate Table. No post-application exposure is expected for the proposed use. There are currently no registered uses of this chemical for use in residential situations. Table 7 summarizes the use pattern of pyridate.

No chemical specific data is available to assess potential exposure to workers. Therefore, this exposure assessment was done using PHED v1.1 data. HED's exposure assessment is based on the assumptions in Table 8.

Table 8. Assumptions for Worker Exposure Assessments

Factors	Quantities/Units
Mixer/Loader and Applicator body weight	70 kg
Estimated acres treated per day	private applicator: 250 acres [1] commercial applicator: 1,000 acres [1]
Applicator unit exposure from PHED; (Groundboom; liquid spray; open cab- single layer with gloves). MEDIUM & HIGH CONFIDENCE DATA	Dermal - 14 µg/lb a.i. handled[2] Inhalation - 0.74 µg/lb a.i. handled[2]
Mixer/loader unit exposure from PHED, (In support of Groundboom; open mixing of liquid, single layer with gloves). HIGH CONFIDENCE DATA	Dermal - 23 µg/lb a.i. handled[2] Inhalation - 1.2 µg/lb a.i. handled[2]

[1] Assumptions regarding acreage treated per day from Personal Communication from R. Lundy, Mint Industry Research Council, 4/8/99.

[2] Source: Pesticide Handlers Exposure Database (PHED) V1.1, Surrogate Exposure Table.

b. Post-Application Exposures

Post-application activities related to mint consist of scouting and mechanical harvesting (Personal Communication from R. Lundy (Mint Industry Research Council) to D. Vogel, 4/8/99). Therefore, there is minimal potential for post-application exposure.

3. Occupational Exposure Assessment

An MOE of 100 is adequate to ensure protection for handler exposures to pyridate via the dermal and inhalation routes. Based on use patterns, only short-term exposure is expected. Since pyridate is applied twice per year, intermediate and long-term exposures from the proposed uses are not expected. Pyridate has not been classified by the HIARC or the Cancer Peer Review Committee (CPRC). However, there is no evidence of a tumorigenic response in the 2-year rat feeding study and the mouse carcinogenicity study with pyridate. Therefore, a cancer risk assessment is not required.

a. Mixer/Loader/Application Exposure Assessment

Table 9 summarizes the HED estimates for dermal exposure for handlers including mixer/loaders, and applicators. In order to present conservative exposure estimates, all exposure calculations were done for commercial applicators. Since private applicators/handlers cannot treat as large an area in a single day, it is assumed that the commercial applicator will have higher exposure than the private applicator.

Table 9. Handler Exposure to Tough 5EC (55.8% Pyridate)

Job Function	Unit Exposure[1] (µg/lb a.i)	AR (lbs ai/Acre)	Acres/ Day	Average Dermal Daily Dose (ADD)[2] (mg/kg/day)	Average Inhalation Daily Dose (ADD)[2] (mg/kg/day)	Total Exposure (mg/kg/day)	MOE [3]
Mixer/ Loaders	Dermal - 23 Inhalation - 1.2	0.94	1000	6.2E-02	1.6E-02	7.7E-02	260
Applicators	Dermal - 14 Inhalation - 0.74	0.94	1000	3.8E-02	9.9E-03	4.8E-02	420

MOE = NOAEL/ADD; (where NOAEL = 20 mg/kg/day, for short-term dermal and inhalation (oral equivalent))
[1] Source: Pesticide Handlers Exposure Database (PHED) V1.1, Surrogate Exposure Table.
[2]ADD = Unit exposure(ug/lb ai) x AR x 1000 Acres/Day x 1/BW (70kg) x % Absorption (100% - inhalation, 20% - dermal)
[3] MOE =NOAEL/Total Exposure

As presented in Table 9, the MOEs are 260 and greater for all handling activities. Therefore, since HED's level of concern for pyridate is for MOEs less than 100, exposure to handlers is below the level of concern.

b. Post-Application Exposure Assessment

Since no potentially significant post-application exposure is expected, this exposure assessment was not performed.

c. Restricted Entry Interval (REI)

For the requested uses, the Worker Protection Standard (WPS) REI of 24 hours based on acute toxicity category II is sufficient to protect workers performing re-entry activities for the proposed use of pyridate.

d. Incident Reports

A compilation of unconfirmed cases of crop/plant damage was submitted by the registrant Novartis. However, it cannot be determined if these cases apply specifically to pyridate.

OTHER CONSIDERATIONS

Metabolism in Plants and Animals

1. The nature of the pyridate residue in plants and ruminants is adequately understood. The total toxic residue consists of pyridate (O- (6-chloro-3-phenyl-4-pyridazinyl) -S-octyl-carbonothioate), its metabolite 6-chloro-3-phenyl-pyridazine-4-ol (aka CL9673), and conjugates of that metabolite, all expressed as pyridate.

Analytical Enforcement Methodology

2. A total residue method using UV/HPLC is available for residue data gathering and enforcement purposes. The method has been adequately validated by recovery data, has passed a successful method trial, and has been forwarded to FDA for publication in PAM-II. The limit of quantitation is 0.03 ppm.

Magnitude of the Residues

3. Residues of pyridate, its metabolite 6-chloro-3-phenyl-pyridazine-4-ol and conjugates of that metabolite all expressed as pyridate are not expected to exceed 0.3 ppm in/on peppermint, tops (leaves and stems) and spearmint, tops (leaves and stems). Time-limited tolerances should be established at this level.

4. Secondary residues are not expected in animal commodities as no feed items are associated with this Section 18 use.

Rotational Crop Restrictions

5. A confined accumulation in rotational crops study with pyridate has previously been submitted and accepted by EFGW/EFED. Pyridate residues metabolize rapidly in soil. No crop rotation label restrictions are needed.

International Residue Limits

6. There are no CODEX, Mexican, or Canadian MRLs established for pyridate in/on mint. Therefore, no compatibility problems exist for the proposed tolerances. See Attachment 2.

SUPPLEMENTAL INFORMATION

DIETARY EXPOSURE

Table 10. Residue Consideration Summary Table

PARAMETER	PROPOSED USE	RESIDUE DATA
CHEMICAL	Pyridate	Pyridate
FORMULATION	Tough 5EC	Tough 3.75EC
CROP	Mint	Mint

Table 10. Residue Consideration Summary Table		
PARAMETER	**PROPOSED USE**	**RESIDUE DATA**
TYPE APPLICATION	Ground only	Ground
# APPLICATIONS	2	2
TIMING	Postemergence with minimum between application interval of 14 days	Post-emergence.
RATE/APPLICATION	0.94 lbs. ai/A	0.08-0.9 lbs. ai/A
RATE/YEAR or SEASON	1.9 lbs. ai/A/[yr]	1.6-1.8 lbs. ai/A/[yr]
MAXIMUM RESIDUE	n/a	0.22 ppm
RESTRICTIONS	PHI of 49 days	PHI of 39-48 days
RESIDUE DATA SOURCE	n/a	this submission
PERFORMING LAB	n/a	not reported

ADDITIONAL INFORMATION

Animal Feedstuffs Considerations. Secondary residues are not expected in animal commodities as no feed items are associated with this Section 18 use.

Progress Toward Registration. IR-4 is in the progress of submitting an application for a Section 3 permanent registration for this use.

Reregistration Status. Pyridate is not a reregistration lists chemical.

Processed Byproducts. Results from a mint processing study were reported. Residues of pyridate did not concentrate in oil.

Attachment 1: DEEM Run: J. Rowell, 5/10/99.
Attachment 2: Codex Request Form.

cc (w/o attachments): D. Vogel, W. Dykstra, G. Kramer, J. Rowell.
RDI: M. Morrow (5/12/99), Team (5/4/99), RAB1 Chemists (5/6/99), G. Kramer (4/29/99)
J. Rowell:806W:CM#2:(703)305-5564:7509C:RAB1

ATTACHMENT 1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 10-MAY-1999

SUBJECT: **Pyridate - Corrected Acute and Chronic Dietary Exposure Analyses.** PP#: 99MT0012. Chemical#: 128834. DP Barcode: D255654. Case #: 291638. Submission #: S558560.

FROM: Jennifer E. Rowell, Chemist
RAB1/HED (7509C)

THROUGH: William H. Donovan, Ph.D., Chemist
RAB1/HED (7509C)

David Soderberg, Chemist
RCAB/HED (7509C)

Melba Morrow, D.V.M., Branch Senior Scientist
RAB1/HED (7509C)

TO: George F. Kramer, Ph.D., Chemist
RAB1/HED (7509C)

Action Requested

Provide an estimate of the dietary exposure and associated risk for pyridate resulting from existing tolerances and proposed tolerance level for residues on mint (PP# 99MT0012). The petitioner proposes the establishment of time-limited tolerances for the residues of pyridate in or on the following raw agricultural commodities (RACs):

Peppermint, tops (leaves and stems)	-	0.3 ppm
Spearmint, tops (leaves and stems)	-	0.3 ppm

Tolerances have been established for the residues of pyridate (40 CFR §180.462) in or on cabbage at 0.03 ppm; chickpeas at 0.1 ppm; corn, fodder at 0.03 ppm; corn, forage at 0.03 ppm; corn, grain at 0.03 ppm; corn, silage at 0.03 ppm; and peanut, nutmeat at 0.03 ppm.

Note: The previous dietary exposure estimate was performed in conjunction with this Section 18 (Memo, J.

Rowell 4/14/99; Barcode D254602) without considering the following RACs: peppermint, peppermint oil, spearmint, and spearmint oil. These commodities have been included in the this dietary exposure estimate.

Executive Summary

Acute and chronic dietary exposure analyses for pyridate were performed using the Dietary Exposure Evaluation Model (DEEM™). Acute and chronic dietary exposure analyses were performed using tolerance level residues and 100% crop treated (CT) information for all commodities. All dietary risk estimates are below the Agency's level of concern for the U.S. population and sub-populations (including infants and children).

Toxicological Endpoints

On October 21, 1997, the Health Effects Division's Hazard Identification Review Committee (HIARC) met to evaluate the toxicology data base of pyridate with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to pyridate as required by the Food Quality Protection Act (FQPA). In addition, the Committee also re-assessed the doses and endpoints selected for acute dietary, chronic dietary (RfD) as well as occupational and residential exposure risk assessments (Memo, J. Rowland 11/3/97). A summary of the toxicological endpoints chosen by HIARC is listed in Table 1.

Acute
Acute RfD = 0.20 mg/kg/day. For acute dietary risk assessment, the HIARC recommended use of the systemic NOAEL of 20 mg/kg/day based on neurotoxic effects (ataxia and emesis) seen at 60 mg/kg/day (LOAEL) in the 90-day feeding study in dogs (MRID# 40101604). An uncertainty factor of 100 (10x for interspecies differences and 10x for intraspecies variations) was used to determine the acute RfD of 0.20 mg/kg/day.

Chronic
Chronic RfD = 0.11 mg/kg/day. For chronic dietary risk assessment, a NOAEL of 10.8 mg/kg/day was used based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL) in a 2-year feeding study in rats (MRID# 00137289, -90, 00138638). An uncertainty factor of 100 (10x for interspecies differences and 10x for intraspecies variations) was incorporated. This was supported by the parental systemic toxicity NOAEL and LOAEL established in the three-generation reproduction study in rats (MRID# 0072347). In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations).

Table 1. Summary of Toxicological Endpoint Selection

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL= 20 UF = 100	Clinical signs indicative of neurotoxicity characterized as ataxia and emesis were observed within 1-3 hours post-dosing on the first day and persisted for duration of study. LOAEL = 60 mg/kg/day.	90-Day Feeding Study - Dog
		Acute RfD = 0.20	
Chronic Dietary	NOAEL = 10.8 UF = 100	Based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL) in a 2-year feeding study in rats. (This was supported by the parental systemic toxicity NOAEL and LOAEL established in the three-generation reproduction study in rats. In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations)).	Chronic Toxicity/Carcinogenicity Study - Rat
		Chronic RfD = 0.11	
Short-Term (Dermal)	NOAEL= 20	See Acute Dietary.	90-Day Feeding Study - Dog
Intermediate-Term (Dermal)	NOAEL= 20	See Acute Dietary.	90-Day Feeding Study - Dog
Long-Term (Dermal)	NOAEL= 10.8	See Chronic Dietary.	Chronic Toxicity/Carcinogenicity Study - Rat
Short Term (Inhalation)	NOAEL= 20	See Acute Dietary.	90-Day Feeding- Dog
Intermediate Term (Inhalation)	NOAEL= 20	See Acute Dietary.	90-Day Feeding- Dog
Long Term (Inhalation)	NOAEL= 10.8	See Chronic Dietary.	Chronic Toxicity/Carcinogenicity- Rat

FQPA Recommendation

On April 5,1999, the FQPA Safety Factor Committee (SFC) met and determined that the 10x factor to account for enhanced sensitivity of infants and children should be removed. **Please note: the decisions made at this meeting for this chemical are applicable only to this Section 18 request** (Memo, B. Tarplee 4/8/99).

The Population Adjusted Dose (PAD) is a modification of the acute or chronic RfD to accommodate the

FQPA Safety Factor. The PAD is equal to the acute or chronic RfD divided by the FQPA Safety Factor. **Since the HED FQPA SFC determined to remove the 10x safety factor, the RfD is identical to the PAD.**

Cancer
Pyridate has not been evaluated by the Cancer Peer Review Committee. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97).

Residue Information

Tolerances for pyridate are published in 40 CFR §180.462. For the acute and chronic analyses, tolerance level residues and 100% CT information were used for all commodities. Default processing factors were used for both the acute and chronic analyses. A summary of the residue information used in the acute and chronic analyses is attached (Attachment 1).

Results/Discussion

The DEEM™ analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-91 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity.

Acute Dietary Exposure Analysis
The acute dietary exposure analysis estimates the distribution of single-day exposures for the U.S. population and certain subgroups and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of pyridate for the commodities on which pyridate is used.

A Tier 1 acute analysis was performed using published and proposed tolerance levels and 100% CT information for all commodities (Attachment 1). For acute dietary risk, HED's level of concern is >100% aPAD. Dietary exposures and associated acute risk at the 95th percentile are shown in Table 2. The other subgroups included in Table 2 represent the highest dietary exposures for their respective subgroups (i.e., children, females, and the other general population subgroups higher than U.S. population). A full listing of dietary exposures is attached (Attachment 2).

Table 2- Summary of Results of Acute DEEM Analysis for Pyridate at the 95th Percentile.

Subgroups	Exposure (mg/kg/day)	% aPAD
U.S. Population (48 states)	0.000139	0.1
Non-Hispanic Blacks	0.000159	0.1
Non-nursing Infants (<1 yr)	0.000278	0.1
Children (1-6 years)	0.000269	0.1
Females (13+/nursing)	0.000124	0.1

The results of the acute analysis indicate that the acute dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

Chronic Dietary Exposure Analysis

The chronic dietary exposure analysis used mean consumption (3-day average) data. A Tier 1 analysis was performed using published and proposed tolerance level residues and 100% CT information for all commodities. For chronic dietary risk, HED's level of concern is 100% cPAD. Dietary exposures for the General Population and other subgroups are presented in Table 3. The other subgroups included in Table 3 represent the highest dietary exposures for their respective subgroups (i.e., children, females, and the other general population subgroups higher than U.S. population). A full listing of chronic dietary exposures is attached (Attachment 3).

Table 3. Summary of Results from Chronic DEEM Analysis of Pyridate.

Subgroups	Exposure (mg/kg/day)	% cPAD
U.S. Population (48 states)	0.000044	0.0
Non-Hispanic Blacks	0.000050	0.0
Non-nursing Infants	0.000121	0.1
Females 13-19 (not preg or nursing)	0.000043	0.0
Males 13-19 yrs	0.000054	0.0

The results of the chronic analysis indicate that the chronic dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

Cancer Dietary Exposure Analysis

Pyridate has not been evaluated by the Cancer Peer Review Committee. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97). Therefore, no cancer dietary exposure analysis was performed.

Conclusions

The acute analysis was performed using published and proposed tolerance levels and 100% CT information for all commodities (Attachment 1). The %aPADs were <100%, and the highest was 0.14% for non-nursing infants (<1 year). For acute dietary risk, HED's level of concern is 100% aPAD. The results of the acute analysis indicate that the acute dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

For the chronic analysis, a Tier 1 analysis was performed using published and proposed tolerance level residues and 100% CT information for all commodities. The %cPADs for all subgroups were <100%, and the highest was 0.1% for non-nursing infants. The results of the chronic analysis indicate that the chronic dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

Pyridate has not been evaluated by the Cancer Peer Review Committee. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97). Therefore, no cancer dietary exposure analysis was performed.

Attachment 1: Pyridate Residue File for Acute and Chronic DEEM™ Analyses.
Attachment 2: Pyridate Acute DEEM™ Analysis (J. Rowell, 30-APR-1999).
Attachment 3: Pyridate Chronic DEEM™ Analysis (J. Rowell, 30-APR-1999).

cc (w/attachments): J.Rowell (RAB1); M.Sahafeyen (CEB1)
RDI: DRES Team [W. Donovan (5/6/99), D. Soderberg (4/30/99)]; M.Morrow (5/10/99)
J.Rowell:806W:CM#2:(703)305-5564:7509C:RAB1

Attachment 1: Pyridate Residue File for Acute and Chronic DEEM™ Analyses.

Filename: C:\JRDeem\Pyridate\128834.r96
Chemical name: Pyridate
RfD(Chronic): .11 mg/kg bw/day NOEL(Chronic): 10.8 mg/kg bw/day
RfD(Acute): .2 mg/kg bw/day NOEL(Acute): 20 mg/kg bw/day
Date created/last modified: 04-30-1999/11:02:38/8 Program ver. 6.73
Comment: Pyridate on mint - G. Kramer. The FQPA Safety Factor was removed, therefore the PAD and RfD are the same.

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
259	6C	Beans-dry-garbanzo/chick pea	0.100000	0	1.000	1.000	
170	5A	Cabbage-green and red	0.030000	0	1.000	1.000	
383	5B	Cabbage-savoy	0.030000	0	1.000	1.000	
267	15	Corn grain-bran	0.030000	0	1.000	1.000	
266	15	Corn grain-endosperm	0.030000	0	1.000	1.000	
289	15	Corn grain-oil	0.030000	0	1.000	1.000	
268	15	Corn grain/sugar/hfcs	0.030000	0	1.500	1.000	
388	15	Corn grain/sugar-molasses	0.030000	0	1.500	1.000	
403	O	Peanuts-butter	0.030000	0	1.890	1.000	
940	O	Peanuts-hulled	0.030000	0	1.000	1.000	
293	O	Peanuts-oil	0.030000	0	1.000	1.000	
310	O	Peppermint	0.300000	0	1.000	1.000	
311	O	Peppermint-oil	0.300000	0	1.000	1.000	
312	O	Spearmint	0.300000	0	1.000	1.000	
313	O	Spearmint-oil	0.300000	0	1.000	1.000	

Attachment 2: Pyridate Acute DEEM™ Analysis (J. Rowell, 30-APR-1999).

U.S. Environmental Protection Agency Ver. 6.73
DEEM ACUTE analysis for PYRIDATE (1989-92 data)
Residue file: 128834.r96 Adjustment factor #2 NOT used.
Analysis Date: 04-30-1999/11:10:15 Residue file dated: 04-30-1999/11:02:38/8
Acute Reference Dose (aRfD) = 0.200000 mg/kg body-wt/day
NOEL (Acute) = 20.000000 mg/kg body-wt/day
Run Comment: Pyridate on mint - G. Kramer. The FQPA Safety Factor was removed, therefore the PAD and RfD are the same.

Summary calculations:

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9th Percentile Exposure	% aRfD
U.S. pop - all seasons:	0.000139	0.07	0.000244	0.12	0.000407	0.20
Hispanics:	0.000149	0.07	0.000250	0.13	0.000422	0.21
Non-hispanic whites:	0.000135	0.07	0.000234	0.12	0.000410	0.20
Non-hispanic blacks:	0.000159	0.08	0.000279	0.14	0.000379	0.19
Non-hispanic other:	0.000128	0.06	0.000250	0.13	0.000594	0.30
All infants (<1 year):	0.000277	0.14	0.000411	0.21	0.000657	0.33
Nursing infants (<1 year):	0.000095	0.05	0.000142	0.07	0.000186	0.09
Non-nursing infants (<1 yr):	0.000278	0.14	0.000442	0.22	0.000682	0.34
Children (1-6 years):	0.000269	0.13	0.000392	0.20	0.000726	0.36
Children (7-12 years):	0.000180	0.09	0.000249	0.12	0.000356	0.18
Females (13+/preg/not nsg):	0.000082	0.04	0.000121	0.06	0.000200	0.10
Females (13+/nursing):	0.000124	0.06	0.000177	0.09	0.000194	0.10
Females (13-19 yrs/np/nn):	0.000109	0.05	0.000147	0.07	0.000320	0.16
Females (20+ years/np/nn):	0.000081	0.04	0.000130	0.07	0.000238	0.12
Females (13-50 years):	0.000092	0.05	0.000137	0.07	0.000268	0.13
Males (13-19 years):	0.000134	0.07	0.000209	0.10	0.000308	0.15
Males (20+ years):	0.000085	0.04	0.000132	0.07	0.000211	0.11
Seniors (55+):	0.000074	0.04	0.000117	0.06	0.000212	0.11

Attachment 3: Pyridate Chronic DEEM™ Analysis (J. Rowell, 30-APR-1999).

U.S. Environmental Protection Agency Ver. 6.74
DEEM Chronic analysis for PYRIDATE (1989-92 data)
Residue file name: C:\JRDeem\Pyridate\128834.r96 Adjustment factor #2 NOT used.
Analysis Date 04-30-1999/11:04:58 Residue file dated: 04-30-1999/11:02:38/8
Reference dose (RfD, CHRONIC) = .11 mg/kg bw/day
COMMENT 1: Pyridate on mint - G. Kramer. The FQPA Safety Factor was removed, therefore the PAD and RfD are the same.

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000044	0.0%
U.S. Population (spring season)	0.000043	0.0%
U.S. Population (summer season)	0.000046	0.0%
U.S. Population (autumn season)	0.000045	0.0%
U.S. Population (winter season)	0.000042	0.0%
Northeast region	0.000041	0.0%
Midwest region	0.000045	0.0%
Southern region	0.000046	0.0%
Western region	0.000043	0.0%
Hispanics	0.000044	0.0%
Non-hispanic whites	0.000043	0.0%
Non-hispanic blacks	0.000050	0.0%
Non-hisp/non-white/non-black)	0.000041	0.0%
All infants (< 1 year)	0.000092	0.1%
Nursing infants	0.000023	0.0%
Non-nursing infants	0.000121	0.1%
Children 1-6 yrs	0.000105	0.1%
Children 7-12 yrs	0.000076	0.1%
Females 13-19(not preg or nursing)	0.000043	0.0%
Females 20+ (not preg or nursing)	0.000028	0.0%
Females 13-50 yrs	0.000032	0.0%
Females 13+ (preg/not nursing)	0.000031	0.0%
Females 13+ (nursing)	0.000036	0.0%
Males 13-19 yrs	0.000054	0.0%
Males 20+ yrs	0.000032	0.0%
Seniors 55+	0.000026	0.0%
Pacific Region	0.000041	0.0%

ATTACHMENT 2

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name: (O- (-chloro-3-phenyl-4-pyridazinyl) -S-octyl-carbonothioate)	Common Name: pyridate	X Proposed tolerance □ Reevaluated tolerance □ Other	Date: 03/26/99

Codex Status (Maximum Residue Limits)	U. S. Tolerances
□ No Codex proposal step 6 or above □ No Codex proposal step 6 or above for the crops requested	Petition Number: 99MT0012 DP Barcode: D254479 Other Identifier:
Residue definition:	Reviewer/Branch: G.F. Kramer
	Residue definition: parent + its metabolite 6-chloro-3-phenyl-pyridazine-4-ol, and conjugates of that metabolite, all expressed as pyridate

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		peppermint, tops (leaves and stems)	0.3
		spearmint, tops (leaves and stems)	0.3

Limits for Canada	Limits for Mexico
□ No Limits □ No Limits for the crops requested	□ No Limits □ No Limits for the crops requested
Residue definition:	Residue definition:

Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions:.

13544

003010

Chemical:	**Pyridate**
PC Code:	**128834**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**05/13/2000**
File ID:	**DPD254479**
Accession Number:	**412-01-0084**

HED Records Reference Center
01/19/2001